

## CLAIMS

*What is claimed is:*

1. A method of suppressing a masking agent, comprising suppressing the interference of a masking agent on a molecular assay of a nucleic acid-containing test sample by contacting  
5 said test sample with an amount of a divalent metal chelator and an amount of at least one chelator enhancing component, the amounts of said divalent metal chelator(s) and said chelator enhancing component(s) being selected such that said masking agents are suppressed.
2. The method of claim 1, wherein said divalent metal chelator is selected from the group  
10 consisting of ethylenediaminetetraacetic acid, imidazole, ethylene*bis*(oxyethylenenitrilo)]tetraacetic acid, [ethylene*bis*(oxyethylenenitrilo)]tetraacetic acid; iminodiacetate; or 1,2-*bis*(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid; *bis*(5-amidino-2-benzimidazolyl)methane or salts thereof.
3. The method of claim 1, wherein said divalent metal chelator is selected from the group  
15 consisting of ethylenediaminetetraacetic acid and 1,2-*bis*(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid, or salts thereof.
4. The method of claim 1, wherein said amount of said divalent metal chelator is about 0.001M to 0.1M.
5. The method of claim 1, wherein said amount of said divalent metal chelator is at least about  
20 0.01M.
6. The method of claim 1, wherein said chelator enhancing component is selected from the group consisting of lithium chloride, guanidine, sodium salicylate, sodium perchlorate and sodium thiocyanate.
7. The method of claim 6, wherein said chelator enhancing component is selected from the  
25 group consisting of sodium perchlorate, sodium thiocyanate, and lithium chloride.
8. The method of claim 1, wherein said amount of said chelator enhancing component is in the range of from about 0.1M to 2M.
9. The method of claim 1, wherein said amount of said chelator enhancing component is at least about 1M.

10. The method of claim 1, wherein said masking agent is selected from the group consisting of leukocyte esterases and heme proteins.
11. The method of claim 10, wherein said heme protein is selected from the group consisting of myoglobin and hemoglobin analogs, and oxidation and breakdown products thereof.
- 5 12. The method of claim 1, wherein said masking agent is selected from the group consisting of ferritins, methemoglobin, sulfhemoglobin and bilirubin.
13. The method of claim 1, wherein said masking agent is selected from the group consisting of methemoglobin and bilirubin.
14. The method of claim 1, wherein said nucleic acid-containing test sample is further  
10 contacted with an amount of at least one enzyme inactivating component selected from the group consisting of manganese chloride, sarkosyl, and sodium dodecyl sulfate in the range of about 0-5% molar concentration.
15. The method of claim 1, wherein said nucleic acid is selected from the group consisting of DNA, RNA, mRNA, and cDNA.
- 15 16. The method of claim 15 wherein said DNA is eukaryotic DNA.
17. A method of improving the signal response of a molecular assay, comprising suppressing the interference of a masking agent on a molecular assay of a nucleic acid-containing test sample by contacting said test sample with an amount of a divalent metal chelator and an amount of at least one chelator enhancing component, the amounts of said divalent metal  
20 chelator(s) and said chelator enhancing component(s) being selected such that said masking agents are suppressed; extracting molecular analytes of interest from said preserved test sample; and conducting a molecular assay on said extracted molecular analytes of interest, wherein the signal response of said molecular assay is improved.
18. The method of claim 17, wherein said divalent metal chelator is selected from the group  
25 consisting of ethylenediaminetetraacetic acid, imidazole, ethylene*bis*(oxyethylenenitrilo)]tetraacetic acid, [ethylene*bis*(oxyethylenenitrilo)]tetraacetic acid; iminodiacetate; or 1,2-*bis*(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid; *bis*(5-amidino-2-benzimidazolyl)methane or salts thereof.

19. The method of claim 17, wherein said divalent metal chelator is selected from the group consisting of ethylenediaminetetraacetic acid and 1,2-bis(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid, or salts thereof.
20. The method of claim 17, wherein said amount of said divalent metal chelator is about 0.001M to 0.1M.
21. The method of claim 17, wherein said amount of said divalent metal chelator is at least about 0.01M.
22. The method of claim 17, wherein said chelator enhancing component is selected from the group consisting of lithium chloride, guanidine, sodium salicylate, sodium perchlorate and sodium thiocyanate.
23. The method of claim 22, wherein said chelator enhancing component is selected from the group consisting of sodium perchlorate, sodium thiocyanate, and lithium chloride.
24. The method of claim 17, wherein said amount of said chelator enhancing component is in the range of from about 0.1M to 2M.
25. The method of claim 17, wherein said amount of said chelator enhancing component is at least about 1M.
26. The method of claim 17, wherein said masking agent is selected from the group consisting of leukocyte esterases and heme proteins.
27. The method of claim 26, wherein said heme protein is selected from the group consisting of myoglobin and hemoglobin analogs, and oxidation and breakdown products thereof.
28. The method of claim 17, wherein said masking agent is selected from the group consisting of ferritins, methemoglobin, sulfhemoglobin and bilirubin.
29. The method of claim 17, wherein said masking agent is selected from the group consisting of methemoglobin and bilirubin.
30. The method of claim 17 wherein said nucleic acid-containing test sample is further contacted with an amount of at least one enzyme inactivating component selected from the group consisting of manganese chloride, sarkosyl, and sodium dodecyl sulfate in the range of about 0-5% molar concentration.
31. The method of claim 17 wherein said nucleic acid-containing test sample is a bodily fluid.

32. The method of claim 20 wherein said bodily fluid is selected from the group consisting of urine, blood, blood serum, amniotic fluid; cerebrospinal and spinal fluid; fluid; synovial fluid; conjunctival fluid; salivary fluid; vaginal fluid; stool; seminal fluid; lymph; bile; tears, and sweat.
- 5 33. The method of claim 32 wherein said bodily fluid is urine.
34. The method of claim 32 wherein said nucleic acid is selected from the group consisting of DNA, RNA, mRNA, and cDNA.
35. The method of claim 34 wherein said DNA is eukaryotic DNA.
36. The method of claim 17 wherein said molecular assay is the polymerase chain reaction.
- 10 37. A method of improving hybridization of nucleic acids, comprising contacting a test nucleic acid with a reagent comprising an amount of at least one divalent metal chelator; and an amount of at least one chelator enhancing component, the amounts of said divalent metal chelator(s) and said chelator enhancing component(s) being selected such that hybridization is improved, such that a test solution is formed; and contacting the test solution with a
- 15 target nucleic acid under conditions favorable for hybridization, such that hybridization occurs.
38. The method of claim 37, wherein said divalent metal chelator is selected from the group consisting of ethylenediaminetetraacetic acid, imidazole, ethylene*bis*(oxyethylenenitrilo)]tetraacetic acid, [ethylene*bis*(oxyethylenenitrilo)]tetraacetic acid; iminodiacetate; or 1,2-*bis*(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid; *bis*(5-amidino-2-benzimidazolyl)methane or salts thereof.
- 20 39. The method of claim 37, wherein said divalent metal chelator is selected from the group consisting of ethylenediaminetetraacetic acid, ethylene*bis*(oxyethylenenitrilo)tetraacetic acid and 1,2-*bis*(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid, or salts thereof.
- 25 40. The method of claim 37, wherein said amount of said divalent metal chelator is about 0.001M to 0.1M.
41. The method of claim 37, wherein said amount of said divalent metal chelator is at least about 0.01M.

42. The method of claim 37, wherein said chelator enhancing component is selected from the group consisting of sodium perchlorate, sodium thiocyanate, and lithium chloride.

43. The method of claim 37, wherein said amount of said chelator enhancing component is in the range of from about 0.1M to 2M.

5 44. The method of claim 37, wherein said amount of said chelator enhancing component is at least about 1M.

45. The method of claim 37 wherein said nucleic acid-containing test sample is further contacted with an amount of at least one enzyme inactivating component selected from the group consisting of manganese chloride, sarkosyl, and sodium dodecyl sulfate in the range of about 0-5% molar concentration.

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46. The method of claim 37 wherein said nucleic acid is selected from the group consisting of DNA, RNA, mRNA, and cDNA.

47. The method of claim 46 wherein said DNA is eukaryotic DNA.

48. The method of claim 1, wherein said amplification is the polymerase chain reaction.

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49. A kit for conducting a polymerase amplification reaction comprising a reagent for suppressing the interference of a masking agent on a molecular assay of a nucleic acid-containing test sample such that when a masking agent is present in a nucleic acid-containing sample subjected to a polymerase amplification reaction said masking agents are suppressed; and instructions for use.